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| 10/770,467 | 02/04/2004 | Bodo Plachter | 966927-20002D | 1358 |

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| EXAMINER | |
|---|---|
| HUMPHREY, LOUISE WANG ZHIYING | |
| **ART UNIT** | **PAPER NUMBER** |
| 1648 | |
| **MAIL DATE** | **DELIVERY MODE** |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/770,467 | PLACHTER, BODO | |
| | Examiner | Art Unit | |
| | Louise Humphrey, Ph.D. | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *26-29 and 31-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *26-29, 33 and 34* is/are allowed.

6)☒ Claim(s) *31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This Office Action is in response to the amendment filed 06 February 2007. Claims 1-25 and 30 are cancelled. Claim 34 is added. Claims 26-29 and 31-34 are pending. Claims 26-29, 33 and 34 are allowable.

Examiner left a message with Applicant's representative, Mr. Christopher Aniedobe, on 19 April 2007, notifying the allowable subject matter. During a telephone interview with Mr. Aniedobe on 23 April 2007, Examiner proposed an amendment to place this application in condition for allowance as follows:

Cancel claims 31 and 32.

Amend claim 26 as follows:

26. A method for producing viral particles comprising the following steps:

(a) provision of a gene-deleted HCMV, wherein the gene of the major capsid protein (UL86) is deleted in the HCMV genome,

(b) transfection of a mammalian cell line with the gene-deleted HCMV from step (a),

(c) replication of the gene-deleted virus from (a) in cells from (b),

(d) infection of mammalian cells with a virus which has been replicated as in steps (a) – (c),

(e) isolation of viral particles from cells which have been infected as in step d), wherein: (i) the particles are surrounded by a lipid membrane in which viral glycoproteins are embedded, and (ii) the particles contain neither viral DNA nor capsids.

## Claim Objections

The objections to claims 31 and 32 are **withdrawn** in response to Applicant's amendment.

## Double Patenting

The Examiner notes with appreciation that Applicants have filed a terminal disclaimer. The nonstatutory double patenting rejection of claims 31 and 32 as being unpatentable over claims 1-14 of US Patent No. 6,713,070 will be withdrawn once Applicants' terminal disclaimer is approved.

## Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 26, 27 and 33 under 35 U.S.C. §103(a) as being obvious over Michel *et al.* (1996) in view of Gibson *et al.* (1984) is **withdrawn** in response to the amendment of claim 26.

The rejection of claims 28 and 29 under 35 U.S.C. §103(a) as being obvious over Michel *et al.* (1996) in view of Gibson *et al.* (1984) and further in view of Uyttersprot *et al.* (1998) is **withdrawn** in response to the amendment of claim 26.

The rejection of claims 31 and 32 under 35 U.S.C. §103(a) as being obvious over Gibson *et al.* (1984) in view of Platchter *et al.* (1990) and Reschke *et al.* (1999) is **maintained**.

The instant claim is drawn to a composition for immunization against HCMV diseases and infections comprising sub-viral particles and pharmaceutically acceptable carrier, wherein the sub-viral particles additionally contain a fusion protein comprising one or more parts of the T-cell antigen pp65 (UL83) and one ore more parts of one ore more proteins which are not pp65.

Examiner's rejection in the Action mailed on 05 June 2006 is as follows:

Gibson *et al.* describe the isolation of noninfectious HCMV particles including dense bodies, which are devoid of capsids and contain less than trace amounts of viral DNA but contain all of the glycoprotein species present in virions. See page 321, last paragraph. Gibson *et al.* specifically describe the use of the noninfectious viral particles as subunit vaccines, which encompass the claimed immunization composition with a pharmaceutical carrier. Gibson *et al.* do not describe a sub-viral particle containing a pp65 fusion protein.

Plachter *et al.* describe fusion protein resulting from fusing different fragments of the open reading frame coding for pp65 with fragments from purified lambda clones. See Abstract and Figure 2. Plachter *et al.* disclose propagation of the virus and purification of HCMV virions or dense bodies from infected primary human foreskin fibroblast cells. See p.1229, Materials and Methods. Plachter *et al.* specifically disclose that pp65 has the potential to elicit an antibody response during natural infection. This protein is a major constituent of the virus particle and represents over 90% of the protein mass of dense bodies. See p.1229, left column, 2nd ¶. The tegument protein pp65 might be one major target of the cell-mediated immune response during natural infection with HCMV. It also causes a humoral immune response in animals as well as in humans. Most importantly, pp65 alone is not a reliable antigen to generate antibody reactivity but might be very helpful in combination with other antigens for the detection of acute stages of HCMV infections. See p.1234, last ¶. Therefore, Plachter *et al.* explicitly suggest fusing pp65 with another immunogen or epitope.

Reschke *et al.* describe humoral immune response to gpUL75 (gH) (Abstract) and constitutive expression of HCMV gH protein in astrocytoma cells (p.252, RESULTS).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the dense bodies of Gibson *et al.* by adding pp65 fused to the gH protein. One having ordinary skill in the art would have been motivated to do this so that the viral particles have increased immunogenicity by eliciting both humoral and CTL immune response. There would be a reasonable expectation of success, given that pp65 and gH proteins can be stably expressed in mammalian cell line, as taught by Plachter *et al.* and Reschke *et al.* Thus, claims 31 and 32 are obvious over Gibson et al. in view of Plachter *et al.* and Reschke *et al.*

Applicant argues that: (1) Plachter *et al.* produced pp65 in a bacterial expression system, without suggestion that it can also be practiced with a mammalian expression system; (2) Plachter *et al.* teach use of pp65 as a sero-diagonistic tool. There is no suggestion or teaching in Plachter *et al.* to use fusion proteins comprising pp65 in the manner claimed in the present invention to immunize patients against HCMV diseases.

Applicant's arguments have been fully considered but are not persuasive. Since HCMV naturally infects human cells, one skilled in the art would have a reasonable expectation of success in expressing this human CMV virus protein in a mammalian expression system. A serodiagnosis involves detecting an antigen with an antibody. The suggestion by Plachter *et al.* (1990) to combine pp65 with other HCMV proteins for serodiagnosis implies that pp65, alone is not a reliable antigen though, can enhance the antigenicity of other HCMV proteins. One skilled in the art would be motivated by this property of pp65 to fuse it with another HCMV protein.

### *Conclusion*

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

### *Contact Information*

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
27 April 2007

Louise Humphrey, Ph.D.
Assistant Examiner